PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	What causes prescribing errors in children? Scoping review
AUTHORS	Conn, Richard; Kearney, Orla; Tully, Mary; Shields, Michael; Dornan, T

VERSION 1 - REVIEW

REVIEWER	Hanan Khalil Khalil Monash University
REVIEW RETURNED	04-Mar-2019

GENERAL COMMENTS	Thank for the opportunity to review your manuscript. I have a few comments for you to consider; 1. Please include a separate section about stakeholders consultation in your results 2. Please expand the discussion section to include more details about differences between adult and children. Best wishes

REVIEWER	Kelly O'Brien University of Toronto, Canada
REVIEW RETURNED	05-Apr-2019

GENERAL COMMENTS	The purpose of this study was to explore the causes of prescribing errors in children. Authors conducted a scoping review (or study) using the Arksey and O'Malley Framework, including the optional consultation phase (Stage 6). Overall the methodology was well done. Authors provide a rationale for choosing a scoping review methodology. They clearly outlined the steps of the Arskey and O'Malley Framework and rationale for conducting the optional consultative phase. The consultative phase, which is often left out of scoping (literature) reviews is a particular strength of this study and should be noted in the discussion. Specific strengths of the review include the clear operational definition of 'causes'; clearly defined eligibility criteria; and the study screening and selection process, which involved 2 reviewers reviewing 100 results jointly (although it was unclear why this process was not done independently); and having all team members independently review 20 abstracts for inclusion. Authors

	nicely adhered to the Arskey and O'Malley framework, and the PRISMA ScR guidelines for reporting of scoping reviews. Authors nicely embedded the qualitative data into the synthesis, which was well described in the methods and reported in the results using the table with supporting quotations. The tables are comprehensive and well described. The 6 causes presented in Figure 2 and tabular format embedded with the text with reference to quotations and included studies nicely triangulate the quantitative and qualitative data and demonstrate how the synthesis led to the resulting 6 causes of prescribing errors. Below are a few minor comments for consideration that largely pertain to the discussion and abstract: • Discussion - have authors considered that the systematic reviews included may have included primary studies also included the study? Is it possible that there was some evidence 'overlap' or 'duplication' of evidence in the review? For instance, is it possible that some causes may have been overemphasized in the results if reported in both primary and overlapping secondary evidence of the included studies? A statement of how might authors might have accounted for this in their synthesis and how it might influence the interpretation of results would be beneficial. • Discussion – some further discussion of generalizability (or transferability) of findings would be beneficial. For instance, authors nicely outline the countries in which the studies were conducted, and in the case of systematic reviews, the countries where these reviews were published. It would be helpful for authors to discuss the diversity of geographical representation of the included studies, the dates (or timing in which these literature were published) and how causes of prescribing errors may differ across different geographical contexts with different health systems and clinical practice models and how the evidence or prescribing medications among children may have changed over the years. • Discussion – The search is up to February 2018 and while I do not suggest authors conduct updated search of the literature, it would be worth mentioning that there may be studies published since the search was completed in the limitations section. • Results – suggest moving the discussion of Figure 1 to the beginning of the results section and adding a paragraph that describes the process of going from the number of citations yielded from the search, to the final 68 studies included in the review. • Abstract – suggest authors add further detail in the abstract that highlights the steps of the Arksey and O'Malley Framework, specifically outlining each of the 6 stages. • Abstract – Study Design section - suggest revising the design section stating that 'authors conducted a scoping review using Arksey and O'Malley Framework including the stakeholder consultation.' • Abstract – Results section – indicate the number of stakeholders in the focus group consultation. • Abstract - the final statement in the conclusion section of the abstract is not supported by the results in the abstract (suggest delete). • Suggest adding the focus group consultation discussion guide as a supplemental file. • References – add the PRISMA-ScR guidelines to the study reference list • Another helpful reference on methodology of scoping reviews that highlights the rationale for conducting scoping reviews and the

	steps that authors might consider for their methodology is Peters et al: http://joannabriggs.org/assets/docs/sumari/Reviewers-Manual_Methodology-for-JBI-Scoping-Reviews_2015_v2.pdf Overall this is a well justified and executed scoping review.

REVIEWER	John Hayden Royal College of Surgeons in Ireland, Ireland
REVIEW RETURNED	27-May-2019

GENERAL COMMENTS	Thank you for the invitation to review this manuscript. The review examines the heterogeneous literature on prescribing errors in paediatrics and maps causes of prescribing errors unique to children. The research question is interesting. The scoping review methodology is appropriate and the review brings together a disparate literature. My suggestions to improve the manuscript: Abstract: Overall OK : Consider flipping the sentence structure of the last two “Strengths & Limitations” points • The risk of overemphasizing expert opinion was introduced by including …. • Article selection was potentially subjective due to…. Introduction: P6L3 – sentence needs expanding. Is this a meta-analysis result or the result of one cohort, what healthcare setting? Methods: Clearly described Results: the results section highlights a wide breadth of causes of errors in paediatric prescribing. Results: P11L10 – explain what subset this could be? Limitations: is there a sense of the content of the 7 texts without full text content? Would they have been consistent with the scoping review findings? Discussion: The implications for research and practice are limited and do not fully build on the breadth of causes identified in the results. While calculations training is highlighted as needed there are many other action points arising from potential causes of error that could be mentioned. How do we solve problems with confusion on mg/kg/day ?– could this be avoided by different dosage expression? Age-banding advantages/disadvantages could be discussed with this? If double-checking is weak or not performed adequately, should it be abandoned or improved? Do policies around weighing children need to change? Lack of paediatric specific formulations is a highlighted issue in results but not discussed. High level of off-label prescribing found as a cause yet no implications or solutions discussed? Similarly, the variety of strengths of liquid medicines are mentioned as a risk, yet no mention of efforts to harmonize strengths between prescribing centres? If there are problems with how prescriptions are written (e.g. mLs instead of mg), can these be avoided? Electronic prescribing is highlighted as a solution briefly although not discussed. Electronic prescribing systems are themselves a

	generator of errors especially in paediatrics so are not the perfect solution either. Can training regimens be changed to improve experience working with children? Or do we need to restrict those who can prescribe for childen? For research implications- the manuscript outlines wells it sown limitations – although this also sets you up for research implications which are not discussed- most of our data comes from specialist paediatric centres and not primary care for example. Do we need to study this better? Also, do we need more qualitative research if a limitation is most studies have been determinants of error rates? Overall, I feel the discussion implications could be more visionary and map the results section a little better to improve the manuscript further.

VERSION 1 – AUTHOR RESPONSE

(R1 = Reviewer 1; R2 = Reviewer 2; R3 = Reviewer 3)

Sections	Reviewer's comments	Response
Abstract	R2: Abstract – suggest authors add further detail in the abstract that highlights the steps of the Arksey and O'Malley Framework, specifically outlining each of the 6 stages.	Abstract format changed to include 'Methods' section, structured around the six scoping review stages.
Abstract	R2: Abstract – Study Design section - suggest revising the design section stating that 'authors conducted a scoping review using Arksey and O'Malley Framework including the stakeholder consultation.'	Study design updated to mention Arksey and O'Malley Framework.
Abstract	R2: Abstract – Results section – indicate the number of stakeholders in the focus group consultation.	Changed – 'multidisciplinary focus group of six prescribing stakeholders'
Abstract	R2: Abstract - the final statement in the conclusion section of the abstract is not supported by the results in the abstract (suggest delete)	Deleted; abstract conclusion updated to reflect changes to discussion overall.
Abstract	R3: Consider flipping the sentence structure of the last two "Strengths & Limitations" points • The risk of overemphasizing expert opinion was introduced by including …. • Article selection was potentially subjective due to….	Done as suggested.
Introduction	R3: P6L3 – sentence needs expanding. Is this a meta-analysis result or the result of one cohort, what healthcare setting?	I reviewed this article, which was a review article by a subject expert. There was no underpinning evidence to support the statement, so I decided

		that for clarity I would remove this sentence from the introduction.
Results	R1: Please include a separate section about stakeholders consultation in your results	A new sub-section, 'Stakeholder consultation' has been added within results, describing participants' details and contributions. The methods have been updated accordingly, moving information about stakeholders' professions to results, and clarifying that we used purposeful sampling to ensure the full range of professions were represented.
Results	R2: Results – suggest moving the discussion of Figure 1 to the beginning of the results section and adding a paragraph that describes the process of going from the number of citations yielded from the search, to the final 68 studies included in the review.	A description of the article selection process, including common reasons for exclusion, has been added.
Discussion	R1: Please expand the discussion section to include more details about differences between adult and children	Discussion has been altered to make reference to the introduction, which explains that adult error rates and types are different, and to lead into the discussion of the specific differences in prescribing for children that cause errors.
Discussion	R2: The consultative phase, which is often left out of scoping (literature) reviews is a particular strength of this study and should be noted in the discussion.	Thank you for this comment - addressed in (renamed) 'strengths and limitations'
Discussion	R2: Discussion - have authors considered that the systematic reviews included may have included primary studies also included the study? Is it possible that there was some evidence 'overlap' or 'duplication' of evidence in the review? For instance, is it possible that some causes may have been overemphasized in the results if reported in both primary and overlapping secondary evidence of the included studies? A statement of how might authors might have accounted for this in their synthesis and how it might influence the interpretation of results would be beneficial.	Thank you for this important point. In considering it, I rereviewed the included studies. It was interesting note that, often, the secondary studies included spoke of quite different causes of errors than the primary studies, as shown in Table 3. I believe, therefore, that the possible overlap doesn't influence results unduly. It was the case, however, that secondary articles made reference to other influential secondary articles, potentially adding weight to certain studies. I addressed both these points with a much more comprehensive point in limitations, stressing that our study was not suited to assessing the degree to which causes led to errors, and that our stakeholder review brought in

		practitioners to confirm or refute the relevance of findings.
Discussion	R2: Discussion – some further discussion of generalizability (or transferability) of findings would be beneficial. For instance, authors nicely outline the countries in which the studies were conducted, and in the case of systematic reviews, the countries where these reviews were published. It would be helpful for authors to discuss the diversity of geographical representation of the included studies, the dates (or timing in which these literature were published) and how causes of prescribing errors may differ across different geographical contexts with different health systems and clinical practice models and how the evidence or prescribing medications among children may have changed over the years.	Information given in 'Article characteristics' to point out that most articles originate from North America or the UK. Within the discussion, sub-section inserted 'nature of the evidence base' which discusses the impact of geographical representation and care settings on transferability of findings.
Discussion	R3: The implications for research and practice are limited and do not fully build on the breadth of causes identified in the results. While calculations training is highlighted as needed there are many other action points arising from potential causes of error that could be mentioned. How do we solve problems with confusion on mg/kg/day ?– could this be avoided by different dosage expression? Age-banding advantages/disadvantages could be discussed with this? If double-checking is weak or not performed adequately, should it be abandoned or improved? Do policies around weighing children need to change? Lack of paediatric specific formulations is a highlighted issue in results but not discussed. High level of off-label prescribing found as a cause yet no implications or solutions discussed? Similarly, the variety of strengths of liquid medicines are mentioned as a risk, yet no mention of efforts to harmonize strengths between prescribing centres? If there are problems with how prescriptions are written (e.g. mLs instead of mg), can these be avoided?	The discussion has been substantially rewritten, expanding on the implications for practice. A table of recommendations has been added. I hope that all of these valuable points have been addressed through recommendations for further research or practical improvements, supported by selective discussion of existing evidence.

	Electronic prescribing is highlighted as a solution briefly although not discussed. Electronic prescribing systems are themselves a generator of errors especially in paediatrics so are not the perfect solution either. Can training regimens be changed to improve experience working with children? Or do we need to restrict those who can prescribe for childen? For research implications- the manuscript outlines wells it sown limitations – although this also sets you up for research implications which are not discussed- most of our data comes from specialist paediatric centres and not primary care for example. Do we need to study this better? Also, do we need more qualitative research if a limitation is most studies have been determinants of error rates? Overall, I feel the discussion implications could be more visionary and map the results section a little better to improve the manuscript further.	
Discussion - limitations	R2: Discussion – The search is up to February 2018 and while I do not suggest authors conduct updated search of the literature, it would be worth mentioning that there may be studies published since the search was completed in the limitations section.	I have included a point to this effect in limitations.
Discussion - limitations	R3: is there a sense of the content of the 7 texts without full text content? Would they have been consistent with the scoping review findings?	Thank you – I rereviewed these potentially contributory articles, which, based on their abstracts, are similar in content to those within the review. I have described this within limitations.
References	R2: References – add the PRISMA-ScR guidelines to the study reference list	Included within methods - We used the six scoping review stages, as laid out by Arksey and O'Malley,[13] to provide a structure for the methods, and adhered to PRISMA-ScR guidelines.[17]
Supplemental information	R2: Suggest adding the focus group consultation discussion guide as a supplemental file.	I have made reference to this document within Methods and will upload it along with the revised manuscript.

VERSION 2 – REVIEW

REVIEWER	Kelly O'Brien University of Toronto, Canada
REVIEW RETURNED	27-Jun-2019

GENERAL COMMENTS	Overall the authors have comprehensively addressed the reviewer comments and revised the manuscript accordingly. I have only one minor suggested revision for consideration. In the results section, under 'Included and Excluded Articles', suggest that the authors state the final number of articles included in the review in order to complete the description of all stages of the flow diagram (Figure 1). This could be the introductory or final sentence of this section. 'Sixty-eight articles were included in the review (n=68) (Table 3). In the article characteristics section, authors can then introduce by stating, 'Of the 68 included articles, 59 (87%) were published….'.

REVIEWER	John Hayden Royal College of Surgeons in Ireland, Ireland
REVIEW RETURNED	27-Jun-2019

GENERAL COMMENTS	Thank you for the opportunity to review a revised version of this manuscript. My previous comments have been addressed. I believe the references are now out of order and require realignment.